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Multicentric Multiple Pregnancy Study IV: Mortality in Twins - Spontaneuos Versus Artificial Reproductive Techniques

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Abstract

Objective: Both spontaneous and ART twin pregnancies have maternal and fetal risks. In this multi-centered cross-sectional study we aimed to determine prognostic differences between spontaneous and ART twin pregnancies in some centers of our country.

Methods: Demographic data of women delivered between the period of 2003 and 2004, including mean maternal age, parity, fetal and perinatal mortality, gestational week at delivery, mode of delivery and maternal morbidity, fetal or newborn's weight and sex were determined from the questionnaire forms and data obtained from 10 obstetrics centers from different parts of Turkey, including university and Health Ministry training hospitals.

Results: The number of twins among the births in ten centers participated in the study was 818. The percentage of spontaneous twins was 24% whereas in 76% ART was applied. There was no difference in the mean age of mothers between the groups. Mean birth week of spontaneous twins was 35.03±2.58 weeks and mean birth week of ART twins was 34.31±3.51 weeks. The ratio of caeserean section in ART and spontaneous twins were 78.6% and 68.8% respectively. While late second trimester mortality was high in ART group and third trimester mortality was high in spontaneous group, perinatal mortaliy was similar between two groups.

Conclusion: In our study there was no significant difference in the perinatal mortaliy between ART and spontaneous twins.

Keywords: Twin pregnancy, mortality, artificial reproductive techniques, spontaneous.

Çok merkezli çoğul gebelik çalışması IV – Spontan ikizlerdeki mortalitenin yardımla üreme teknikleriyle gebe kalanlardaki ikizler ile karşılaştırılması

Amaç: Hem spontan, hem de yardımla üreme teknikleri (YÜT) sonrası ortaya çıkan çoğul gebelikler maternal ve fetal riskleri beraberinde getirmektedir. Çok merkezli kesitsel olan bu çalışmamızda, ülkemizin bazı merkezlerindeki spontan ve YÜT ikiz gebelikleri arasındaki prognoz farklılığını araştırmayı amaçladık.

Yöntem: Bu çalışma 2003-2004 yılları içinde Türkiye'nin değişik bölgelerinde Üniversite ve Eğitim Araştırma Hastanesi bünyesinde yer alan 10 ayrı Kadın Hastalıkları ve Doğum Merkezine gönderilen anket ve klinik bilgi formları ile yapıldı. Ankette anne yaşı, gebelik ve doğum sayıları, gebe kalış şekli, doğum haftası ve şekli, yenidoğan ağırlığı, cinsiyeti ve mortalitesi, maternal mortalite-morbidite parametreleri sorgulandı.

Bulgular: Çalışmaya katılan 10 merkezdeki toplam ikiz doğum sayısı 818'dir. Bu çoğul gebeliklerin %24'ü spontan olup %76'sına YÜT uygulandı. Gruplar arasındaki anne yaşı ortalamaları arasında fark saptanmadı. YÜT gebeliklerinde ortalama doğum haftası 34.31±3.51 hafta iken, spontan gebelerde 35.03±2.58 hafta idi. YÜT ve spontan gebeliklerdeki sezaryen oranları sırasıyla %78.6 ve %68.8 olarak saptandı. Geç ikinci trimester kayıpları YÜT grubunda, üçüncü trimester kayıpları ise spontan grupta daha fazla gözlenirken, perinatal mortalite her iki grupta benzer bulundu.

Sonuç: Çalışmamızda ikiz gebeliklerde gebeliğin YÜT ya da spontan olması mortalite açısından anlamlı farklılık yaratmamaktadır.

Anahtar Sözcükler: İkiz gebelik, mortalite, yardımcı üreme tekniği, spontan.

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Introduction

Progress in the artificial reproductive techniques (ART) is the cause of the increase of the ratio of multiple pregnancies at the present. The success of centers using induction of ovulation, in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) is measured by the ratio of pregnancy, meanwhile, the real measure, the healthy fetus at term (favorably singleton) is sometimes ignored. Because of the reduced pregnancy rates by the conservative approaches in the favor of Singleton pregnancies and the psychological stress brought by failed pregnancy after a long and expensive treatment processes and to prevent the decrease in the success of the Assisted Reproductive Technique (ART) centers, implementation of aggressive therapies which may result multiple pregnancies are preferred. However, both spontaneous and ART multiple pregnancies are accompanied by maternal and fetal risks.[1-4] Although the increased ratio of multiple pregnancies in our country has been mentioned in many scientific meetings, no comprehensive national study has been planned to determine the factors related to the increase of multiple pregnancies and maternal/fetal mortality and morbidity related to these multiple pregnancies. The comprehensive multi-centered studies related on this subject have been published by the present study group.[5,6] The aim of this cross-sectional multi-center study was to reveal the mortality ratios in the spontaneous and ART twins in various Obstetrics and Gynecology clinics in our country.

Methods

Demographic data of women delivered between the period of 2003 and 2004, including mean maternal age, parity, fetal and perinatal mortality, gestational week at delivery, mode of delivery and maternal morbidity, fetal or newborn's weight and sex were determined from the questionnaire forms and data obtained from 10 obstetrics centers from different parts of Turkey, including university and Health Ministry training hospitals. Some unreported data in the survey were requestioned and the missing ones were completed. Ovulation induction, ICSI and IVF pregnancies have been accepted as assisted reproductive techniques. The term "stillbirth" has been defined for the death of the fetus, who (or any of his twins) is at least 400 grams of weight or who completed 20 th gestational week, before birth or no respiration after birth or no heart beat. The term "early neonatal death" has been defined for neonatal deaths within the first 7 days after birth. The data of spontaneous and ART twin pregnancies were compared using statistical tests of chi-square, Fisher's exact and Student's t-test. SPSS for Windows version 14.0 (SPSS Inc, Chicago, IL, ABD) was used for statistical analyses. The value of $p < 0.05$ was accepted as significant.

Results

The total number of births was 43.258 between 2003 and 2004 in ten centers which participated in the study. The total numbers of twins were 818 (18.9/1000) and the total numbers of triplets was 42 (0.97/1000). The data of type of pregnancy was available in 265 twins and 24.15% of them were spontaneous and in 75.85% of them ART was applied. The demographics of both spontaneous and ART twins are given in the table 1. There was no significant difference in the mean maternal age. The only significant difference was higher number of previous gestations in the spontaneous twin pregnancies as expected. Mean birth weeks were 34.31 ± 3.51weeks in ART twins and 35.03 ± 2.58 weeks in spontaneous twins. The perinatal mortality ratio in the twin pregnancies was 106.9/1000 and the mortality ratio and survival ratios according to the type of pregnancy are given in the Table 2. The chance of being alive of both fetuses was 10% higher in ART twins though not statistically significant. Concerning the type of delivery, the ratio of death of at least one fetus was 7.7% and the ratio of live birth of both fetuses was 92.3% in caesarean section. These ratios were 42.1% and 57.9% in vaginal deliveries. The mortality ratios in births with caesarean section and vaginal deliveries according to the type of pregnancy are given in the Table 3. When the spontaneous and ART twins were compared according to the mean weights of live and dead fetuses, mean weights of ART twins were lesser in all groups. But this difference was found to be statistically significant only in the group where both fetuses were dead (Table 4). Survival ratios were lower in fetuses with weight of

Table 1. Demographics of spontaneous and ART twins.

	Spontaneous	Artificial reproductive techniques	p
Maternal age	27.56±4.40	28.35± 5.10	0.269
No of gestations	2.42 ±1.46	1.98±1.60	**0.048**
Gestational week	35.03±2.58	34.31± 3.51	0.129
Birth weight	2220.55±601.49	2160.78±634.44	0.507

Table 2. Mortality in spontaneous and ART twins.

	Spontaneous	Artificial reproductive techniques	p
Both alive	79.4%	89.5%	0.133
One fetus dead	14.7%	3.9%	0.159
At least one fetus alive	94.1%	93.4%	0.628
Both fetuses dead	5.9%	6.6%	0.399

≤1500 grams in both spontaneous and ART pregnancies (Table 5). When the spontaneous and ART twins were grouped as both living or both deceased or one deceased, mean week of birth was lower in all ART groups. Fetal loss ratio was higher in the late second trimester in ART twins whereas fetal loss ratio was higher in the third trimester in spontaneous twins. Therefore, mean gestational week was significantly lower in the ART twins who both deceased compared to the corresponding spontaneous twin group (Table 6). Live birth ratios were lower in both genders of spontaneous twins compared to ART twins. Survival rates and mortality ratios were similar in both genders of spontaneous pregnancies. However, mortality ratio of female gender was aproximately half of the mortality ratio of male gender in ART pregnancies (p >0.05) (Table 7). Maternal morbidity factors were more in the twin pregnancies with perinatal mortality. However, there was no significant difference between spontaneous and ART pregnancies.

Table 3. Types of pregnancy and delivery in spontaneous and ART twins.

Type of delivery	Type of pregnancy		(%)
Caesarean section	Spontaneous	Both alive	**86.4**
		One fetus dead	13.6
	ART	Both alive	**94.2**
		One fetus dead	4.3
		Both fetuses dead	1.4
Vaginal delivery	Spontaneous	Both alive	**66.7**
		One fetus dead	16.7
		Both fetuses dead	16.7
	ART	Both Alive	**42.9**
		Both fetuses dead	57.1

Discussion

Chorionicity is an important factor for the complications in the twin pregnancies. As, fetal risks like fetal loss, preterm birth or IUGR is higher in the monochorionic pregnancies compared to dichorionic ones.[7] In a study with large numbers of twins reported from our country the ratio of dichorionic pregnancies was 85% and the mortality ratio of these was 6%. The ratio of monochorionic pregnancies was 15% but the mortality ratio of these was 14%.[8] It was not possible to determine the distribution of chorionicity in our study due to design of study and some missing data in the records. Compared to the singleton pregnancies, stillbirths are seen twice more in ART twin pregnancies.[9] However, perinatal prognoses of ART twins are indifference with spontaneous twins and even a little better, though ART twins are more preterm and have lower birth weights.[10-12] It has

Table 4. Birth weights of spontaneous and ART twins.

	Spontaneous		ART		
	Mean	S.D	Mean	S.D	p
Both alive	2238.15	508.93	2153.62	561.70	0.499
One fetus dead	1653.00	180.05	1261.67	828.16	0.325
Both fetuses dead	1705.00	643.47	674.40	280.84	**0.023**

Tablo 5. Mortality in spontaneous and ART twins according to birth weights.

Birth weight	Type of pregnancy	Mortality	Percentage
<1,500 gram	Spontaneous	Both alive	50.0
		One fetus dead	25.0
		Both fetuses dead	25.0
	ART	Both alive	56.3
		One fetus dead	12.5
		Both fetuses dead	31,3
> 1,500 gram	Spontaneous	Both alive	83.3
		One fetus dead	13.3
		Both fetuses dead	3.3
	ART	Both alive	98.3
		One fetus dead	1.7

Table 6. Mortality and gestational weeks in spontaneous and ART twins.

	Gestational week		
Mortality	**Spontaneous**	**ART**	**p**
Both alive	35.52±2.29	34.38±3.03	0.082
One fetus dead	33.20±2.39	31.00±4.36	0.381
Both fetuses dead	34.00±2.83	24.60±3.21	**0.016**

Table 7. Mortality in spontaneous and ART twins according to gender.

Type of pregnancy	Gender		(%) Percentage
Spontaneous	Male	Alive	87.9
		Dead	12.1
	Female	Alive	85.3
		Dead	14.7
ART	Male	Alive	89.9
		Dead	10.1
	Female	Alive	94.4
		Dead	5.6

been suggested that maternal complications, birth weeks and birth weights are not different in such pregnancies.[13] This is explained by that monochorionic twins are encountered rare in ART twins (32% versus 7%) and that the complications occur rarely.[14]. However, in a study from our country comparing 274 ART and 348 spontaneous twins the findings were in conflict. In this twin study preterm birth before 37 weeks and birth weight of ≤2,500 grams were found 20% higher. Preterm birth before 32 weeks and birth weight of ≤1,500 grams were found 40% higher. Perinatal mortality was thrice higher and perinatal morbidity was twice higher and the general prognosis was worse.[15] These were not confirmed by the study of Güney et al only increased EMR and 120 grams lesser mean birth weights were reported in the ART twin pregnancies.[16] The differences in these studies may probably be due to morbidity criteria of the studies and the differences in the monochorionic pregnancy ratios. In a study comparing 112 spontaneous twins and 56 ART twins, Nassar et al reported the ratio of caesarean section as 58% in spontaneous twins and 77% in ART twins. They also reported that preterm birth ratios and respiratory complications related to this were higher in ART group.[17] Vasario et al found no significant difference in neonatal outcomes between 139 spontaneous twins and 84 IVF twins and they found non-significant higher rate of caesarean section in ART group.[18] Similarly, Luke et al found no difference in terms of complications when compared 2,143 spontaneous and 424 ART twin pregnancies.[19] In our study we found no significant effect of ART considering the mortality and survival ratios. We found higher rates of caesarean section and earlier birth weeks and, as a consequence, lesser birth weights in ART twin pregnancies compared to spontaneous twin pregnancies. Though earlier birth weeks in ART twin pregnancies is not statistically significant, this may be due to preference of caesarean section more in ART twin pregnancies. In spite of the fact that no difference was found in the mortality rates between spontaneous and ART twins in our study, it should be kept in mind that multiple pregnancies increase the maternal and fetal risks compared to singleton pregnancies and that implantation of more than three embryos does not increase the chance of live birth instead increase the complications.[1-4,20] In addition, it has been suggested that 4% decrease in perinatal mortality will occur if more than one fetus is prevented in ART.[21]

Conclusion

In our study there was no significant statistical difference in the perinatal mortality between ART and spontaneous twins though the risk was higher in spontaneous twins and male fetuses. However, it is to kept in mind that high numbers of twins due to ART pregnancies will increase the complications compared to the singleton pregnancies.

References

1. Chan FY. Obstetrics implication of multiple gestation. *Aust N Z J Obstet Gynaecol* 2006;46(Supp1):3-13.
2. Lee MY, Cleary-Goldman J, D'Alton ME. Multiple gestations and late preterm (near term) deliveries. *Semin Perinatol* 2006;30:103-12..
3. Huang CT, Au HK, Chien LW, Chang CW, Chien YY, Tzeng CR. Twin pregnancy outcome among cases of spontaneous conceptions, intrauterin insemination, and invitro fertilization/intracytoplasmic sperm injection. *Fertil Steril* 2006;86:1017-9.
4. Reddy UM, Wapner RJ, Rebor RW, Tosca RJ. Infertility, assisted reproductive technology and adverse pregnancy outcomes: executive summary of a National Institute of Child Health and Human Development workshop. *Obstet Gynecol* 2007;109:967-77.
5. Yayla M, Baytur Y. Çok merkezli çoğul gebelik çalışması I: Epidemiyoloji. *Perinatoloji Dergisi* 2008;16:1-8.
6. Yayla M, Baytur Y. Multicentric multiple pregnany study II: Perinatal mortality in twins. *Perinatal Journal* 2009;17:8-17.
7. Sebire NJ, Snijders RJM, Hughes K, Sepulveda W, Nicolaides KH. The hidden mortality of monochorionic twin pregnancies. *Br J Obstet Gynaecol* 1997;104:1203- 7.
8. Yıldırım G, Gül A, Aslan H, Erol O, Güngördük K, Ceylan Y. İkiz gebeliklerde koryonisitenin neonatal ve maternal sonuçlara etkisi. *Türk Jinekoloji ve Obstetrik Derneği Dergisi* 2007;4:178- 83.
9. Pinborg A, Loft A, Nyboe Andersen A. Neonatal outcome in a Danish National Cohort of 8602 children born after in vitro fertilization or intracytoplasmic sperm injection: the role of twin pregnancy. *Acta Obstet Gynecol Scand* 2004;83:1071-8.
10. McDonald S, Murphy K, Beyene J, Ohlsson A. Perinatal outcomes of in vitro fertilization twins: a systematic review and meta-analyses. *Am J Obstet Gynecol* 2005; 193:141-52.
11. Pinborg A. IVF/ICSI twin pregnancies: risks and prevention. *Hum Reprod Update* 2005;11:575-93.
12. Fitzsimmons BP, Bebbington MW, Fluker MR. Perinatal and neonatal outcomes in multiple gestations: assisted reproduction versus spontaneous conception. *Am J Obstet Gynecol* 1998;179:1162-7.
13. Pinborg A, Loft A, Rasmussen S, Schmidt L, Langhoff_Roos J, Greisen G, Andersen AN. Neonatal outcome in a Danish national cohort of 3438 IVF/ICSI and 10,362 non-IVF/ICSI twins born between 1995 and 2000. *Hum Reprod* 2004;19:435-41.
14. Mukopadya N, Arulkumaran S. Reproductive outcomes after in-vitro fertilization. *Curr Opin Obstet Gynecol* 2007;19:113-9.
15. Saygan-Karamürsel B, Tekşam O, Aksu T, Yurdakök M, Önderoğlu L. Perinatal outcomes of spontaneous twins compared with twins conceived through intracytoplasmic sperm injection. *J Perinat Med* 2006;34:132-8.
16. Güney M, Oral B, Mungan T, Özbaşar D. Antepartum, intrapartum and perinatal outcome of twin pregnancies after in vitro fertilization. *J Turkish-German Gynecol Assoc* 2006:7;115-9.
17. Nassar AH, Usta IM, Rechdan JB, Harb TS, Adra AM, Abu-Musa AA. Pregnancy outcome in spontaneous twins versus twins who were conceived through in vitro fertilization. *Am J Obstet Gynecol* 2003;189:513-8.
18. Vasario E, Borgarello V, Bossotti C, Libanori E, Biolcati M, Arduino S, et al. IVF twins have similar obstetric and neonatal outcome as spontaneously conceived twins: a prospective follow-up study. *Reprod Biomed Online* 2010;21:422-8.
19. Luke B, Brown MB, Nugent C, Gonzalez-Quintero VH, Witter FR, Newman RB. Risk factors for adverse outcomes in spontaneous versus assisted conception twin pregnancies. *Fertil Steril* 2004;81:315-9.
20. El-Toukhy T, Khalaf Y, Braude P. IVF results: optimize not maximize. *Am J Obstet Gynecol* 2006;194:322-31.
21. Oakley L, Doyle P. Predicting the impact of in vitro fertilisation and other forms of assisted conception on perinatal and infant mortality in England and Wales: examining the role of multiplicity. *BJOG* 2006;113:738-41.